UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,118	09/09/2003	Hiroyuki Yokoi	242232US0CONT	9226

22850 7590 08/24/2006

C. IRVIN MCCLELLAND
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,118	YOKOI, HIROYUKI	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-16* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/9/03; 12/9/03*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS: 2/16/05*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-11, 15, and 16, with traverse, filed on July 6, 2006 is acknowledged and has been entered. Claims 12-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 1-16 are pending. Claims 1-11, 15, and 16 are under examination.

2. Applicant traversed the restriction requirement on the grounds that no adequate reason or examples have been provided to support conclusion of patentable distinctness between the identified groups or shown that a burden exists in searching all of the claims. Applicant specifically contends that both groups contain the essential procedure of measuring analyte contained in a whole blood sample wherein reaction proceeds in the presence of a detergent and in a state that the cells are not disrupted, i.e. lysed.

In response, Applicant's argument is not persuasive because the dilution and separation steps using different diluents and reagents, are structural and functional requirements in one group that is not required in the other; hence, the search and evaluation of pertinent prior art requires that such structural and functional requirements are given full consideration and met in that one particular group which is not so for the other. Therefore, while searches between the two groups would be expected to overlap

as suggested by Applicant, there is no reason to expect the searches to be coextensive. Accordingly, the restriction requirement is being maintained.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. It is noted that PCT/JP02/002139 filed on March 7, 2002 has been published as WO 2002/073203 on September 19, 2002 in Japanese.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11, 15, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claim 1 is indefinite in reciting, "A method of measuring analyte" because it is unclear as to whether 1) a qualitative measure is intended to be obtained, i.e. presence of analyte, or 2) a quantitative measure is intended to be obtained, i.e. amount of analyte, or 3) a kinetic binding interaction is intended to be obtained. Please clarify.

The phrase, "which comprises" in claim 1 is objected to as, transitional language in claims are recited in active form, i.e. comprising.

Claim 1 is confusing because it is unclear where recited method steps begin and end. It is suggested but not required that method steps should be designated as step a), step b), step c), etc. or should at the very least be recited in separate lines encompassing each distinct separate method step. As an example, claim 1 should recite in distinct method steps:

- forming a reaction system,
- allowing the analyte to react,
- measuring a formed reaction product, etc.

The phrase, "a reaction step of forming a reaction system" appears redundant; hence, rendering the claim indefinite. Perhaps, Applicant intends, "[comprising,] forming a reaction system".

Claim 1 is confusing in reciting, "a sample containing whole blood" because it is unclear what is encompassed by the term "sample" in connection with the recited "whole blood." Specifically, the whole blood should be properly defined as the "whole blood sample" as it is the element suspected of containing the analyte to be measured and not the treatment solution (claim 3) if the recited sample is intended to contain the treatment solution. Alternatively, it is unclear as recited, what other elements are "contained" in the sample other than whole blood. If the sample is intended to contain the treatment solution as aforementioned, it appears, therefore, that the recited

"sample" should clearly be defined as "a sample mixture comprising or consisting of whole blood and a treatment solution". Please clarify. See also claims 4 and 9.

Claim 1 is vague and indefinite in reciting, "a first substance carried by a solid carrier" because it is unclear how the first substance is carried by the solid carrier in relation to the "sample mixture". Perhaps Applicant intends, "a first substance immobilized to a solid carrier." See also claim 15.

Claim 1 is ambiguous in reciting, "... and specifically binding to an analyte contained..." because it is unclear as to whether specific binding between the first substance and a desired specific analyte is intended for measurement. As recited, it appears that any and all recited first substance is/are specifically binding any and all analytes present in the sample. Perhaps, Applicant intends, "... which specifically binds to an analyte contained."

Claim 1 lacks clear antecedent basis in reciting, "analyte contained in the sample" because it is unclear how the recited "a sample" contains the analyte, since the analyte should be expected to be contained in the whole blood. As recited, the recited "a sample" is not whole blood but only contains the whole blood.

Claim 1 is ambiguous in reciting, "a second substance specifically binding to the analyte", because it is unclear as to whether specific binding between the second substance and the desired specific analyte is intended for measurement. As recited, it appears that any and all recited second substance is/are specifically binding any and all analytes present in the sample. Perhaps, Applicant intends, "a second substance specifically binds to the analyte." Same analogous problems and comments apply to all

other occurrences of the recitation of "specifically binding to the analyte" in the claims including claims 4, 8, 11, and 15.

The phrase, "and a measurement step of measuring a reaction product" appears redundant; hence, rendering the claim indefinite. Perhaps, Applicant intends, "and measuring ...".

Claim 1 is indefinite in reciting, "measuring a formed reaction product" because it is unclear as to whether 1) a qualitative measure is intended to be obtained, i.e. presence of analyte, from the "reaction product", or 2) a quantitative measure is intended to be obtained, i.e. amount of analyte, from the "reaction product", or 3) a kinetic binding interaction is intended to be obtained. Please clarify.

Claim 1 is vague and indefinite in reciting, "a formed reaction product" because it is unclear what is encompassed by such recitation in relation to the other elements of the claim. As recited, claim 1 fails to define what structural and functional cooperative relationship exists between the analyte, the first substance with the solid carrier, the second substance, and the recited formed reaction product. Perhaps, Applicant intends that the first substance immobilized to the solid carrier specifically binds to an analyte to form a complex which further binds to the [labeled] second substance; hence, forming the complex which consists the reaction product.

Claim 1 is indefinite in missing a correlation step since the last method step only recites, "measuring a formed product". Accordingly, it is unclear how the claimed method steps provide a measure of (the presence of or amount of) an analyte in the whole blood sample, as required by the preamble.

Claim 1 is confusing in reciting by enumeration, "(1) the reaction step is performed in a state...; and (2) at least the reaction step is performed in the presence of ... a detergent" because such limitations do not encompass method steps but rather, are limitations that appear to intend to delimit the method steps recited. Additionally, it is unclear how "the reaction step is performed in the presence of ... a detergent" since the method steps recited in claim 1 do not appear to provide that "a detergent" is added and allowed to be incubated with the sample mixture. Please clarify. If Applicant intends that the treatment solution which is added to the whole blood comprises the detergent (as in claim 3), then such structural and functional cooperative relationship should be clearly defined in claim 1.

Claims 1 is vague and indefinite in reciting, "can prevent influence" because the term "influence" is a subjective term that lacks a comparative basis of defining its metes and bounds. See also claim 4.

Claim 1 is ambiguous because it is unclear what is encompassed in reciting, "a component existing in the reaction system." Please clarify. See also claim 4.

Regarding claim 2, the phrase "type [detergents]" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "detergent types"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d). See also claim 5.

Claim 4 is non-idiomatic and, therefore, confusing in reciting, "containing" and "contains". It is specifically unclear what other elements are intended to be "contained"

in the sample or in the whole blood. Perhaps, Applicant intends "comprising" and "comprises".

Claim 9 is replete with lacking and improper antecedent basis problems in reciting, "the reaction step of allowing...", "a first reaction step of allowing...", "a first reaction product", "a second reaction step of allowing...", "the first reaction product", and "a second reaction product", since claim 1 from which it depends recites, "a reaction step of forming" and "a formed reaction product". Accordingly, it is unclear what structural and functional cooperative relationships exist between each of the elements and reaction product in claim 1 and all the elements and reaction products recited in claim 9. It is suggested but not required that consistency in terminology and relationship between elements should be maintained between a set of claims in order to render the claims clear and well defined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 recites a method for measuring analyte by combining all of 1) a first substance that is immobilized into a solid phase and that specifically binds to an analyte (i.e. capture antibody or antigen), 2) a second substance that is detectably labeled and that specifically binds to the analyte (i.e. labeled antibody or antigen), and 3) a whole

blood sample suspected of containing the analyte; allowing the first substance, the second substance, and the analyte to undergo a binding interaction so as to form capture substance: analyte: labeled substance complexes; and measuring the amount of the formed complexes. In as far as the recitation of "the reaction step is performed in a state that blood cells are not disrupted", the disclosure at page 14, first full paragraph provides that the "a state that blood cells are not disrupted" is intended to encompass 1) adding a detergent that does not cause hemolysis, 2) regulating osmotic pressure with an isotonic solution such as physiologic saline (i.e. hypotonic solutions cause red cells to cremate and hypertonic solutions cause red cells to swell; hence both instances can cause hemolysis), 3) adding magnesium ions to prevent disruption of cell nuclei. Accordingly, it appears that the recitation of "the reaction step is performed in a state that the blood cells are not disrupted" intends that the blood cells are not caused to be disturbed so as to cause hemolysis. In as far as the recitation of "at least the reaction step is performed in the presence of a sufficient amount of a detergent that does not cause hemolysis, does not inhibit reactions of the analyte with the first and second substances ...", there is no recitation in the recited method steps of any pretreatment or addition or inclusion of a detergent; hence, it is unclear how the assay is performed in the "presence" of a detergent. Accordingly, the limitation of "in the presence of a sufficient amount of a detergent" has not been given patentable weight.

5. Claims 1-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Hoshino et al. (US Patent 6,143,510).

Hoshino et al. disclose a method of quantitatively measuring analyte in undiluted whole blood sample. Watkins et al. specifically disclose contacting the whole blood sample comprising the analyte with a capture antibody (first partner) immobilized into magnetically responsive particulate insoluble carrier, wherein the capture antibody specifically binds the analyte in the whole blood sample, and a labeled detection antibody (second partner) that also specifically binds the analyte in the whole blood sample. The whole blood reaction mixture is incubated for a time period to allow binding interaction between the antibodies and the analyte so as to form capture antibody – analyte – labeled antibody complexes (see Abstract, column 4, lines 4-22 and lines 38-43), and column 5, lines 11-17). According to Hoshino et al., separation steps and washing steps may be performed between the addition of the different binding partners. Hoshino et al. specifically teach washing the reaction mixture with a washing solution containing 0.1% polyoxyethylene sorbitan monolaureate (Tween 20) four times at different times during the procedure. Chemiluminescence intensity of the different complexes formed is measured using a photomultiplier (see column 8, lines 27-36 and Example 3).

Since detergents such as polyoxyethylene sorbitan monolaureate in concentrations of 0.1% as used by Hoshino et al. does not cause hemolysis, does not substantially inhibit analyte-antibody interactions, and has inhibiting effects for non-specific binding by other components in the assay sample, it is deemed that Hoshino et al. inherently anticipates the claimed invention.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

6. Claims 1, 2, 4, 5, and 7-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Watkins et al. (US Patent 6,280,618).

Watkins et al. disclose a heterogeneous assay method of quantitative measurement of analyte in a whole blood sample (see Abstract and column 12, lines 3-5). Watkins et al. specifically disclose combining the whole blood sample with a capture antibody immobilized into magnetic microparticle that specifically binds an analyte in the whole blood sample, and a labeled detection antibody that also specifically binds the analyte in the whole blood sample. The mixture is incubated for a time period to allow binding interaction between the antibodies and the analyte so as to form capture antibody – analyte – labeled antibody complexes (see column 7, line 65 to column 8, line 6 and lines 33-56). Detection of the complexes is performed by flow cytometry (see Abstract, column 3, line 66 to column 4, line 17, and column 11, lines 58-65). Examples of analytes in whole blood to be detected include TSH, T3, and T4 (see column 9, lines 33-39). Watkins et al. also teach adding a wash buffer including 0.01% polyoxyethylene sorbitan monolaureate (Tween 20) into the magnetic microparticles (see Example 1).

Since detergents such as polyoxyethylene sorbitan monolaureate in concentrations of 0.01% as used by Watkins et al. does not cause hemolysis, does not

substantially inhibit analyte-antibody interactions, and has inhibiting effects for non-specific binding by other components in the assay sample, it is deemed that Watkins et al. inherently anticipates the claimed invention.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

7. Claims 1-11, 15, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Ullman et al. (US Patent 6,103,537).

Ullman et al. disclose an electroseparation binding assay method and kit for quantitative measurement of analyte in a whole blood sample (see Abstract). Specifically, Ullman et al. specifically disclose combining the whole blood sample suspected of containing analyte with antibody (first specific binding partner) immobilized into a synthetic particle that specifically binds the analyte in the whole blood sample, and a labeled antibody (second specific binding partner) that also specifically binds the analyte in the whole blood sample. The mixture is incubated for a time period to allow binding interaction between the antibodies and the analyte so as to form synthetic particle antibody – analyte – labeled antibody complexes (see column 3, lines 20-38, column 4, lines 52-63, column 5, lines 48-57, and column 5, line 66 to column 6, line 5). The analyte can be any one of proteins, hormones, and cancer antigens (see column 6, line 6 to column 8, line 26). The synthetic particles used may be any one of dextran

latex , polystyrene, or magnetic particles (see column 13, lines 28-67 and column 18, lines 23-59). Detection of the complexes is performed using different signal producing systems including fluorescent, enzyme, and chemiluminscent labels (see column 11, lines 12-40). Ullman et al. also teach adding surfactants and binding enhancers (i.e. do not substantially inhibit analyte-antibody interactions) or agents that block non-specific binding (i.e. has inhibiting effects for non-specific binding by other components) in the assay medium including proteins or detergents such as polyalkylene glycols, polyoxyethylene sorbitan monolaureate (Tween 20) and Triton X-100. The concentration of the detergent is about 0.01 to 1% by weight (see column 12, lines 21-29, column 14, lines 46-54, and column 18, lines 63-66).

Since detergents such as polyoxyethylene sorbitan monolaureate in concentrations of 0.01 to 1% as used by Ullman et al. does not cause hemolysis, does not substantially inhibit analyte-antibody interactions, and has inhibiting effects for non-specific binding by other components in the assay sample, it is deemed that Ullman anticipates the claimed invention.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

8. No claims are allowed.

Remarks

9. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Sakamoto et al. (US Patent 6,194,219) disclose using polyoxyethylene sorbitan surfactant as cross-linking agent for water insoluble carriers in whole blood heterogeneous immunoassays, and provide that analytical result therefrom does not change the quantity of whole blood in the sample.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
August 21, 2006